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September 1957

ARS-33-42

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UNITED STATES DEPARTMENT OF AGRICULTURE
Agricultural Research Service

SCREENING TESTS OF MISCELLANEOUS COMPOUNDS CONTAINING THE METHYLENEDIOXYPHENYL STRUCTURE

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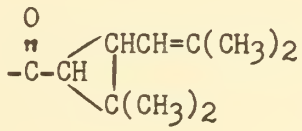
Entomology Research Division

In continuation of our study of derivatives of methylenedioxybenzene (3, 5), we are reporting the preparation, physical properties, and biological effects of some miscellaneous compounds. These derivatives were screened routinely as mosquito larvicides, body louse and chigger toxicants, and mosquito repellents, and some of them as synergists against body lice and house flies.

The names, formulas, physical properties, and methods of preparing these compounds are given in table 1. The general routes of synthesis are outlined on the following pages. Results of the screening tests[1/] are reported in table 2.

All the chrysanthemumoyl esters are dl-cis-trans compounds, and throughout the paper $R''C(=O)-$ represents the chrysanthemumoyl radical—



1/ Carroll N. Smith, M. M. Cole, H. Gouck, and J. C. Keller conducted biological tests. Ray W. Ihndris aided in the preparation of the paper.

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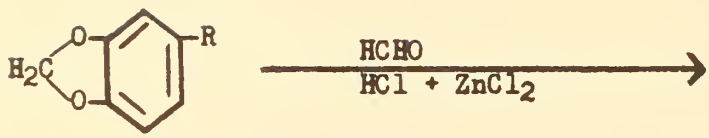
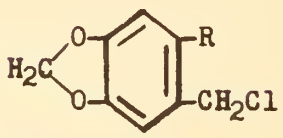
Compounds Derived from Safrole and Isosafrole

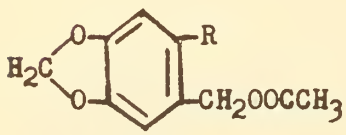


R = allyl (safrole) (ENT-514)
R = propenyl (isosafrole) (ENT-2068)

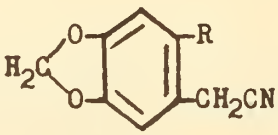


R = allyl (ENT-20963)
R = propenyl (ENT-20875

NaOAc
HOAc

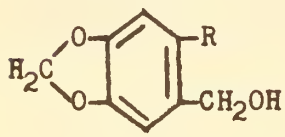


R = allyl (ENT-20909)

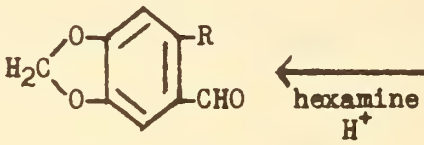


R = allyl (ENT-20962)
R = propenyl (ENT-20989)

NaOMe | MeOH

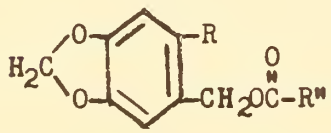


R = allyl (ENT-20906)

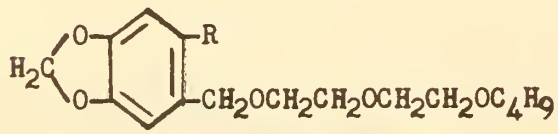


R = allyl (ENT-20907)
R = propenyl (ENT-20988)

pyridine | $R''C(=O)-Cl$

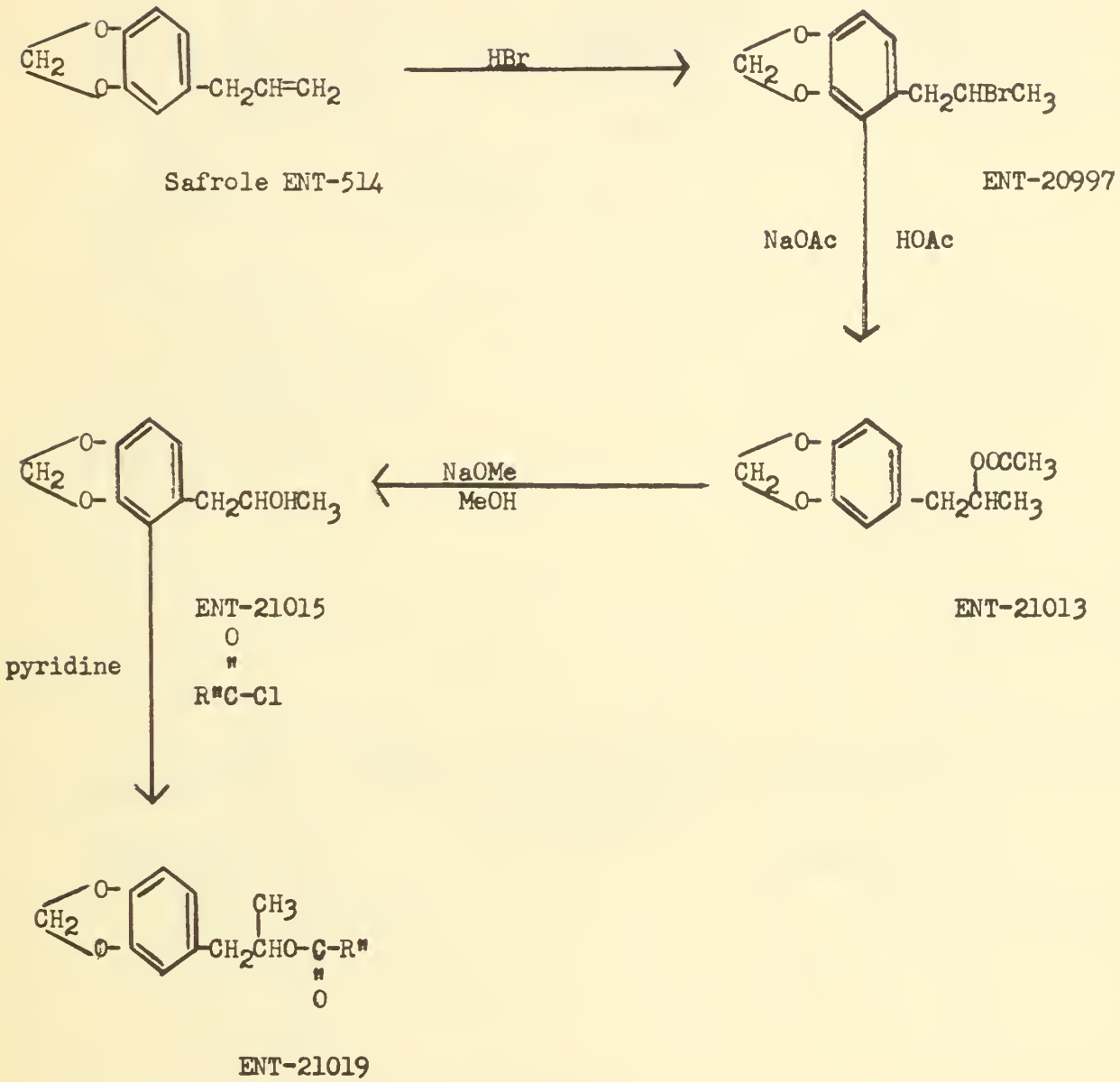


R = allyl (ENT-20908)
R = propenyl (ENT-20717) (from crude intermediate)

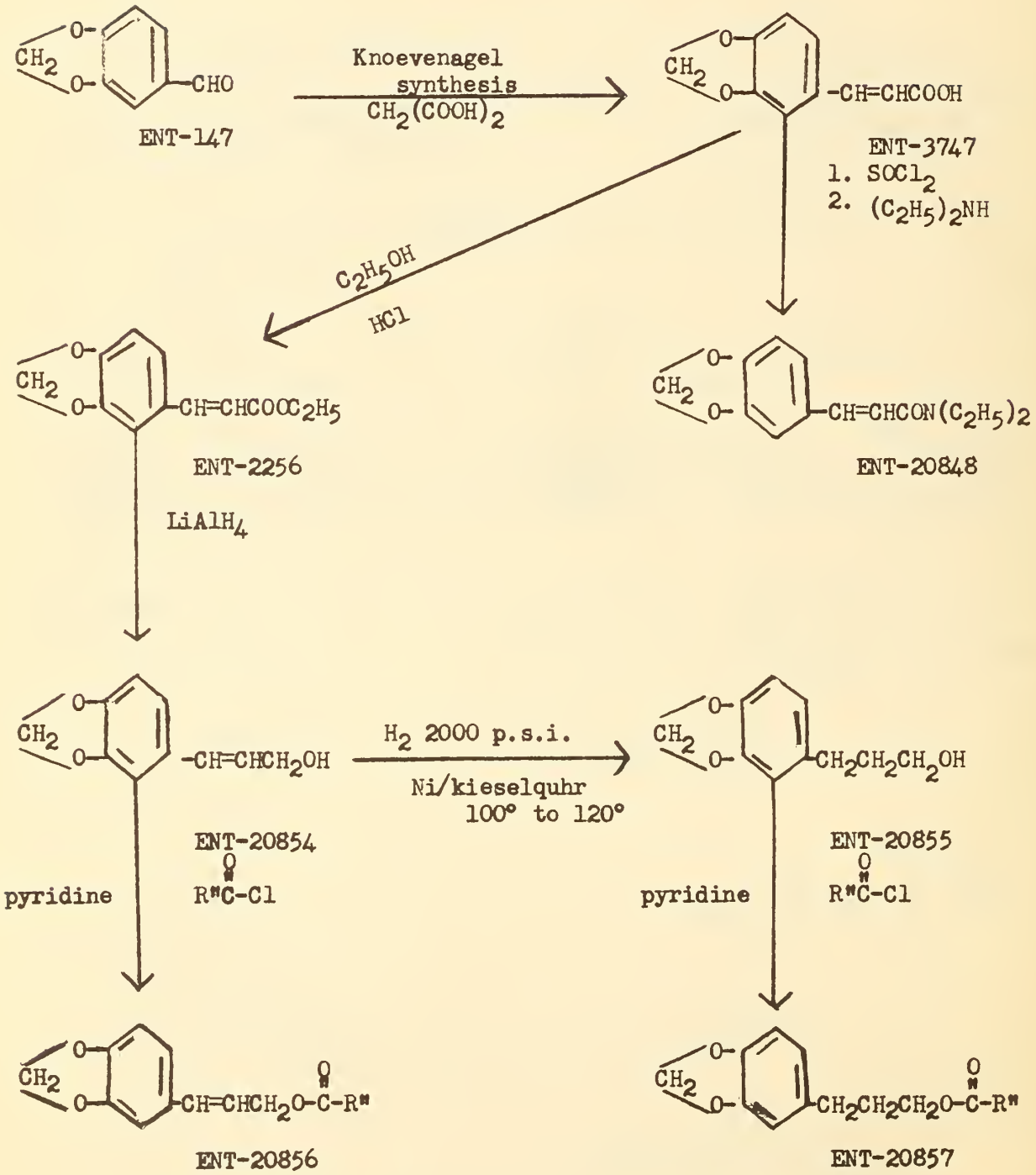


R = allyl (ENT-20964)
R = propenyl (ENT-21029)

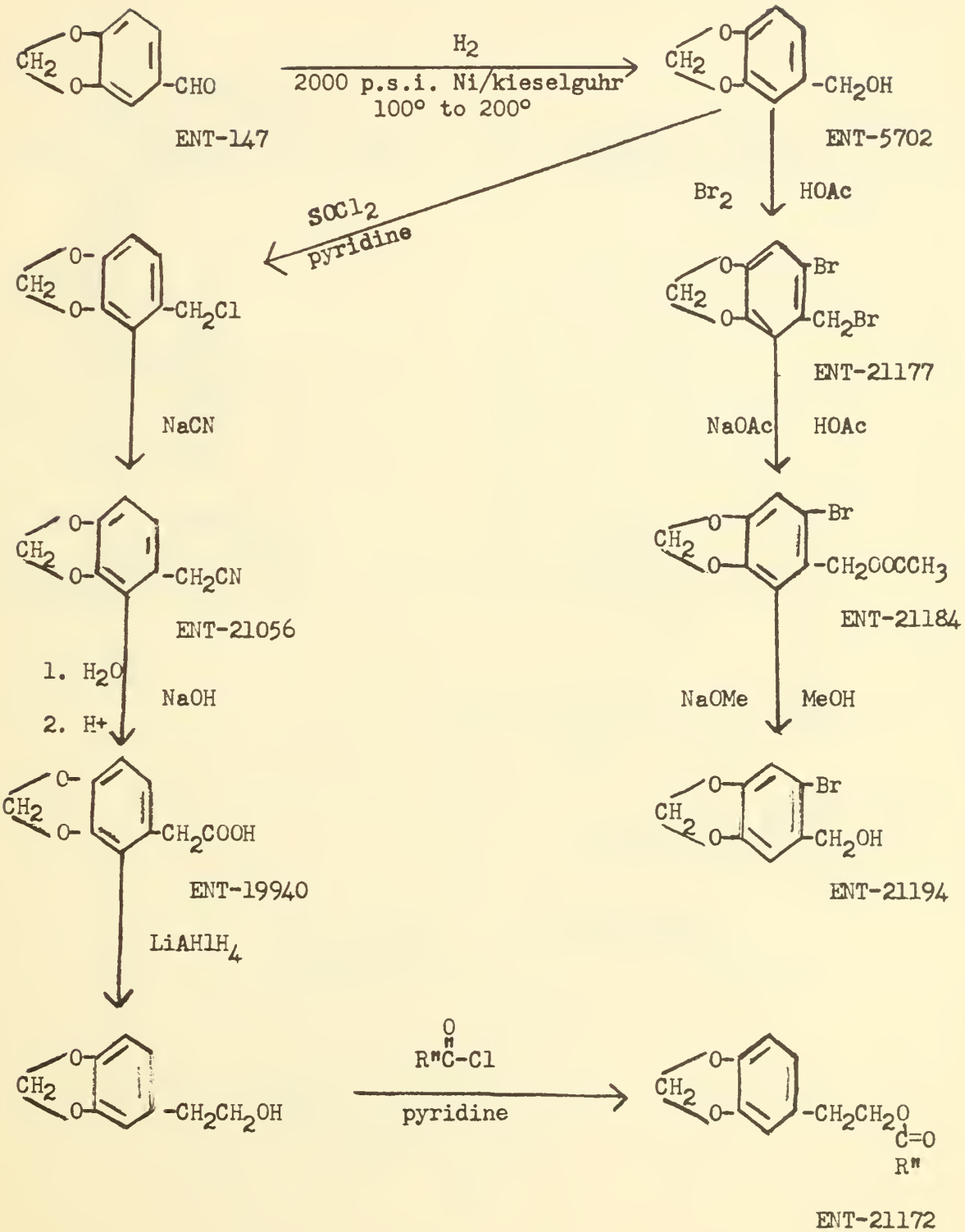
Syntheses Based on the Hydrogen Bromide Addition to Safrole



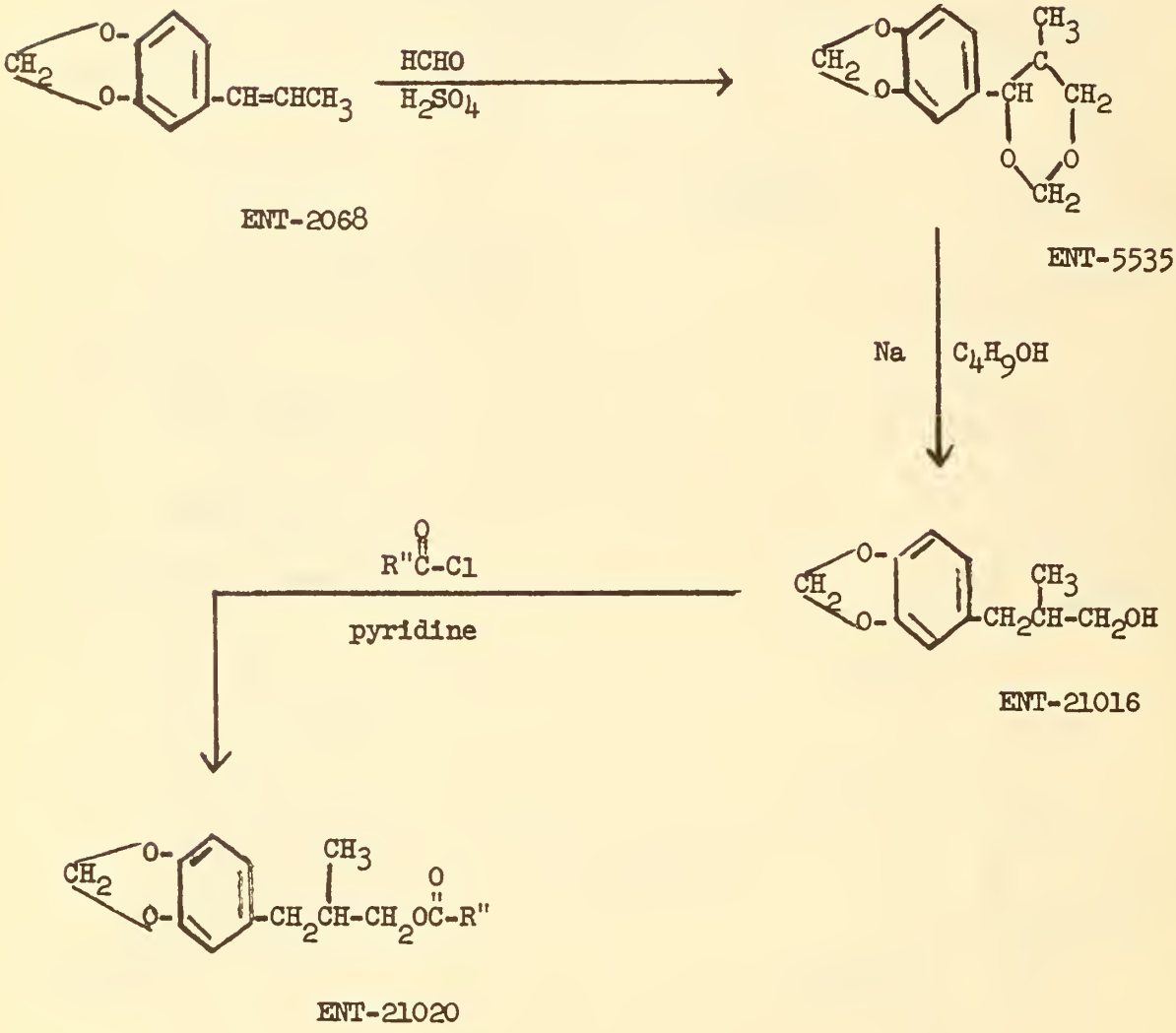
3,4-Methylenedioxycinnamic Acid and Derivatives



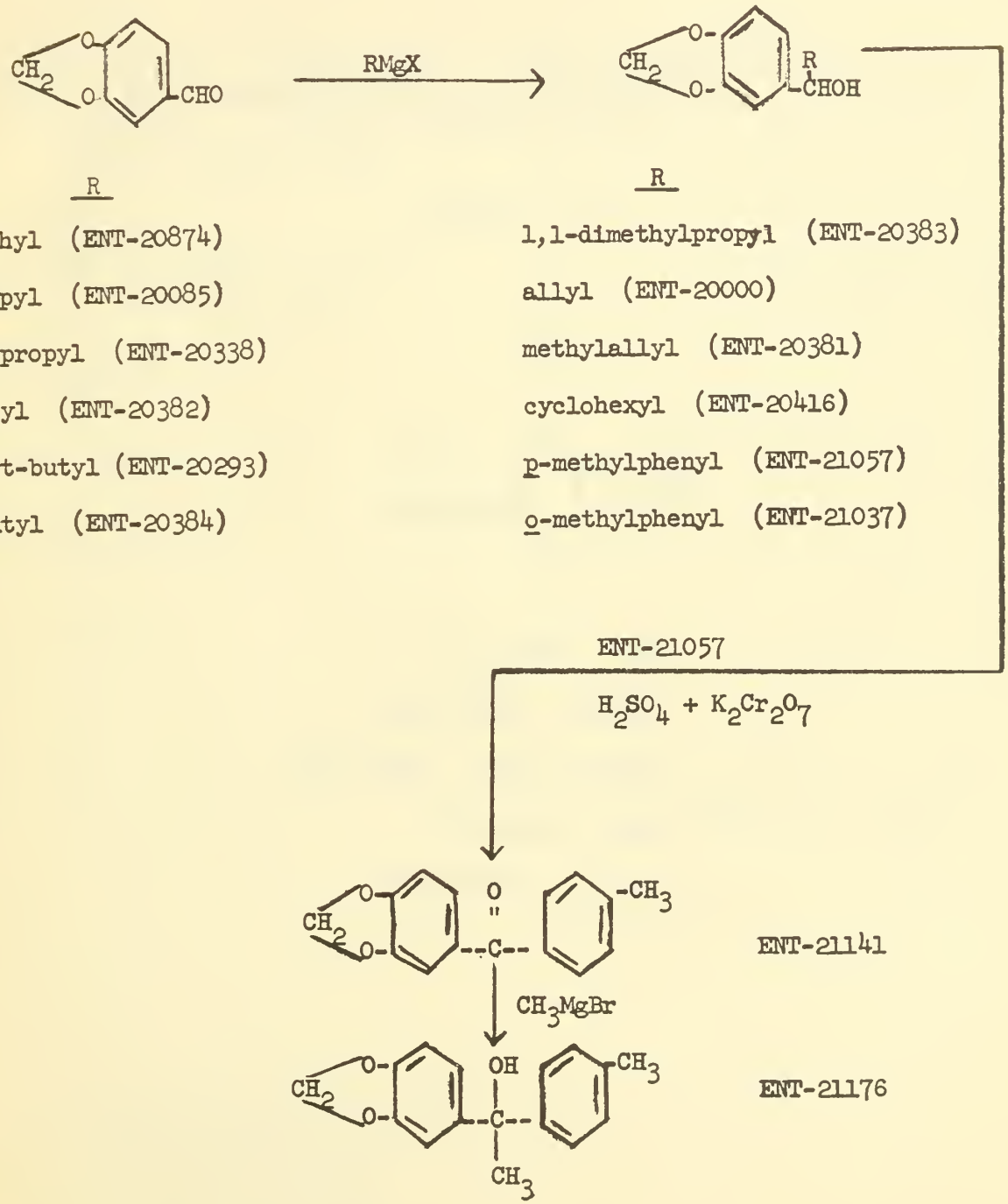
Piperonyl Alcohol and Derivatives



Syntheses Based on the Prins Reaction with Isosafrole

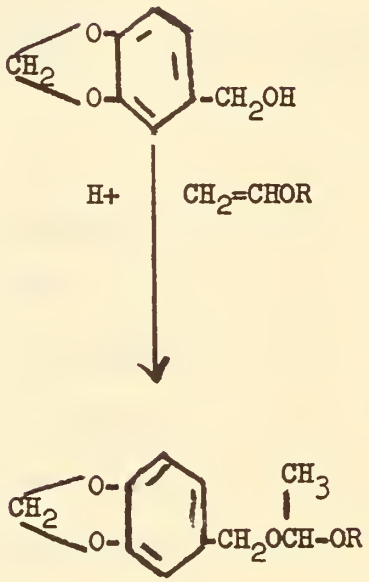


alpha-Substituted Piperonyl Alcohols and Derivatives



R	R
methyl (ENT-20874)	1,1-dimethylpropyl (ENT-20383)
propyl (ENT-20085)	allyl (ENT-20000)
isopropyl (ENT-20338)	methylallyl (ENT-20381)
butyl (ENT-20382)	cyclohexyl (ENT-20416)
tert-butyl (ENT-20293)	p-methylphenyl (ENT-21057)
pentyl (ENT-20384)	o-methylphenyl (ENT-21037)

Acetals of Piperonyl Alcohol



ENT-5702

R

C_2H_5 (ENT-21257)

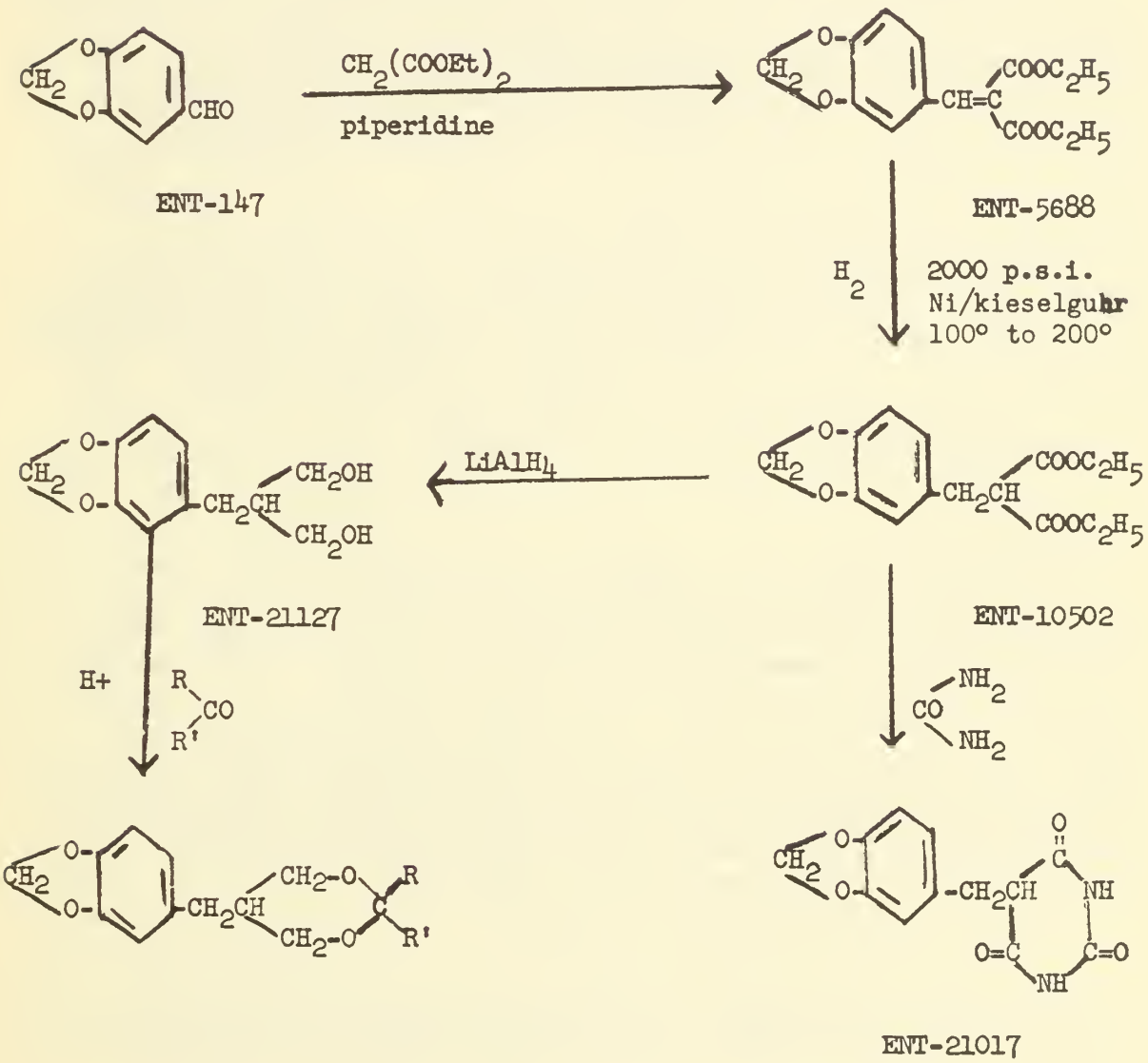
CH_2CH_2Cl (ENT-21274)

$CH_2CH(C_2H_5)C_4H_9$ (ENT-21256)

C_4H_9 (ENT-21275)

iso-C_4H_9 (ENT-21276)

Compounds Derived from Piperonal-Malonic Ester Condensation



Methods of Preparation

A. Chloromethylation

An example of chloromethylation is the preparation of 5-(chloromethyl)-safrole (ENT-20963). Hydrogen chloride gas was introduced during 1½ hours to saturate a well-stirred and cooled mixture of 400 grams of technical safrole, 50 grams of zinc chloride (anhydrous), 240 ml. of 37 percent formalin, and 400 ml. of ethylene dichloride while the temperature was between -2° and 2°C. Approximately 750 ml. of ether was added; the mixture was poured over ice and then transferred to a separatory funnel. The lower aqueous layer was discarded. The ether layer was washed with a saturated sodium chloride solution, then with saturated sodium bicarbonate until neutral, and again with saturated sodium chloride. After drying overnight over calcium chloride, the solvent was removed under vacuum and the residue was distilled. About 75 grams of unchanged safrole was removed up to 116°/6 mm. The temperature then rapidly rose to 148°/3.5 mm., at which point 306 grams (61 percent) distilled. The supercooled liquid had a refractive index of n_D^{25} 1.5637 and after solidification melted at 42° [lit. m.p. 42.5° (10)].

B. Aldehydes

An example of aldehyde formation is the preparation of 6-allyl-piperonal (ENT-20907). Crude ENT-20963 from 200 grams of safrole was refluxed 2 hours with 200 grams of hexamine, 300 ml. of glacial acetic acid, and 300 ml. of water. Then 300 ml. of concentrated hydrochloric acid was added and the mixture refluxed for 20 minutes. After it had stood in a cold-water bath (5°C.) overnight, enough water was added to dissolve the precipitated salt, and the solution was extracted with ether. The ether solution was washed with a saturated sodium bicarbonate solution until neutral, and then with a saturated sodium chloride. The ether was removed and the residue distilled. Unreacted safrole came over first; then the 72 grams of product distilled.

C. Acetates (via the Grignard Synthesis)

An example of an acetate preparation is alpha-(p-methylphenyl) piperonyl acetate (ENT-21039). The Grignard reagent was prepared from 94.1 grams (0.55 mole) of p-bromotoluene and 13.4 grams (0.55 mole) of magnesium. After being started with a little methyl bromide, the reaction went smoothly. No iodine or methyl iodide was used because of an apparent tendency of iodine to favor polymerization during preparation of piperonyl alcohols. When addition of the p-bromotoluene was complete, stirring was continued until refluxing ceased; then 82.6 grams (0.55 mole) of piperonal in 250 ml. of dry benzene was added slowly dropwise to the Grignard with stirring under reflux. After standing overnight, the Grignard was cooled to 0-5°C., with stirring, and 400 ml. of dilute hydrochloric acid added slowly. The mixture was then transferred to a separatory funnel and the aqueous layer drawn off.

The solvent layer was washed consecutively with saturated solutions of sodium chloride, sodium bicarbonate, and sodium chloride. It was then transferred to a distilling flask, and the benzene and ether were removed under vacuum without heating of the residue above 80°. The residue was then warmed for 4 hours on a steam bath with 50 ml. of acetic anhydride and 5 grams of sodium acetate. The reaction mixture was then poured into water and the solution extracted with ether. The ether extract was washed with sodium bicarbonate until neutral and then with saturated sodium chloride. The ether was removed on a steam bath and the residue distilled. Low-boiling material was discarded and 54 grams of the product collected.

D. Alcohols

1. Catalytic reduction. Piperonal (1 mole) in 200 ml. of alcohol at 2000 p.s.i. with 5 grams of nickel on kieselguhr catalyst (Reeve and Sterling (22) used a copper chromite catalyst at 4500 p.s.i.) gave a quantitative yield of piperonyl alcohol.

2. Hydrolyses of the acetate /see Acetates (via the Grignard synthesis)/. The acetate in 10 percent excess of 2N sodium methylate was either refluxed for several hours or allowed to stand overnight at 25°C. The mixture was poured into cold water and extracted with ether. The ether layer was washed with a saturated salt solution and then dried over sodium sulfate. After removal of ether, the residue was distilled.

3. Reduction of acids, esters, and aldehydes to the alcohols with lithium aluminum hydride was carried out in the usual manner (1).

E. Chrysanthemumates

The chrysanthemumates were prepared from the alcohols by the method of Harvill (8) with slight modifications. The preparation of alpha-(p-methylphenyl)-piperonyl chrysanthemumate-(ENT-21030) provides an example. The alcohol (0.10 mole) was dissolved in 100 ml. of dry Skelly A solvent containing pyridine (0.11 mole). Chrysanthemumoyl chloride (0.1 mole) was added slowly at 25-35°C. with continuous stirring. The mixture stood overnight at 25° and then was washed with 5-percent hydrochloric acid and 5-percent sodium hydroxide and saturated sodium chloride. After removal of the solvent the residue was distilled.

F. Ketones

The preparation of 4-methyl-3',4'-methylenedixoybenzophenone (ENT-21141) is an example. Twenty-three grams of ENT-21057 was oxidized by adding it slowly to a stirred solution of 30 grams of sodium dichromate and 25 grams of concentrated sulfuric acid in 150 ml. of water in a beaker. The solution became hot immediately, and stirrring was continued for 1½ hours. When cool it was extracted with ether and the extract washed with water, dried, and the ether removed on a steam bath. The solidified residue was recrystallized from 95-percent ethyl alcohol.

G. Amides

The amides were made from the acid chlorides and excess amine in the usual manner.

H. Acetals

The preparation of 4-(1-ethoxyethoxy)methyl-1,2-methylenedioxybenzene (ENT-21257) is an example. Vinyl ethyl ether[2/] (0.3 mole) was slowly added to a rapidly stirred solution of piperonyl alcohol (0.2 mole) in ethyl ether to which 2 drops of concentrated hydrochloric acid had been added. After being refluxed at 40°-60°C. for 1/2 hour, the solution stood at room temperature for 24 hours. The solution was washed with 5-percent sodium bicarbonate and then with a saturated salt solution. The product was dried over anhydrous sodium sulfate, and after removal of the solvent the residue was distilled.

I. Amines

a. Secondary. The preparation of N-ethylpiperonylamine (ENT-20863) provides an example. This was prepared by hydrogenation at 1800 p.s.i. and 100°C. of 150 grams of piperonal, 62 grams of 70 percent aqueous ethylamine and 200 ml. of alcohol in 1/2 hour. The catalyst was removed by centrifuging, and the alcohol was removed on the steam bath. The residue was distilled to give 144 grams of product.

b. Tertiary. The preparation of N-ethyl-N-propylpiperonylamine (ENT-20864) provides an example. Thirty-four grams of N-ethylpiperonylamine (ENT-20863) were refluxed 3 hours with 25 grams of propyl bromide and 12 grams of potassium hydroxide (85 percent). After cooling the product was taken up in ether. After the ether solution had been washed with saturated sodium chloride, it was dried over sodium sulfate. The ether was removed on the steam bath and the product distilled.

J. Miscellaneous

a. Preparation of 6-[2-butoxyethoxy)ethoxy]methylsafrole (ENT-20964). Forty grams of butyl carbitol was added slowly, with stirring, to 7 grams of sodium hydride covered with ether. An efficient condenser prevented the ether from being swept out by hydrogen. The 50 grams of 6-allylpiperonyl chloride (ENT-20963) was slowly added and the mixture refluxed for 6 hours. After standing overnight, the ether solution was washed with water, dilute hydrochloric acid, and saturated sodium chloride, and then dried. After removal of the ether the product was distilled under high vacuum in a short path still.

2/ The vinyl ethers used in this study were kindly supplied by the Carbide and Carbon Chemical Company.

b. Preparation of 2-piperonyl-1,3-propanediol (ENT-21127). This compound was prepared by the lithium aluminum hydride reduction (1) of the diethyl ester of piperonylmalonic acid (ENT-10502).

c. Preparation of 2-methyl-5-piperonyl-m-dioxan (ENT-21253). This compound was prepared from 2-piperonyl-1,3-propanediol (ENT-21127) and acetaldehyde by the method of Prill et al. (21), except that .5 ml. of 85-percent phosphoric acid per mole of starting material was used as a catalyst instead of p-toluenesulfonic acid.

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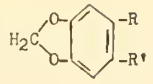
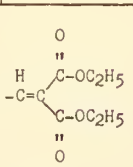
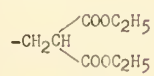
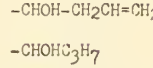
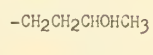
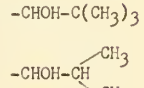
Table 1.--Physical properties and methods of preparation of various compounds containing the methylenedioxyphenyl structure

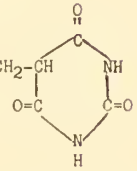
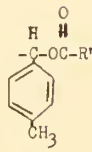


R"C- = chrysanthemumoyl

ENT No.	Empirical formula	Name	R	R'	Yield (%)	Boiling point °C.	Boiling point mm/Hg	Melting point (°C.)	n_D^{25}	Method of preparation
5688	$C_{15}H_{16}O_6$	Malonic acid, piperonylidene, diethyl ester		H	90	-	-	63	-	(14)
5702	$C_8H_8O_3$	Piperonyl alcohol	$-CH_2OH$	H	90	114-15	2	53	-	D (22)
10502	$C_{15}H_{18}O_6$	Malonic acid, piperonyl-, diethyl ester		H	100	185-86	5	-	1.5019	D (14)
16012	$C_{11}H_{14}O_3$	Piperonyl alcohol, 6-propyl-	$-C_3H_7$	$-CH_2OH$	74	173-8	17	-	1.5495	D
16016	$C_{19}H_{20}O_4$	Acetic acid, phenyl-, 6-propylpiperonyl ester	$-C_3H_7$	$-CH_2OOCCH_2C_6H_5$	46	193	2	-	1.5582	A
20000	$C_{11}H_{12}O_3$	Piperonyl alcohol, alpha-allyl-	$-CHOH-CH_2CH=CH_2$	H	82	131	1	-	1.5514	D (2)
20085	$C_{11}H_{14}O_3$	Piperonyl alcohol, alpha-propyl-	$-CHOHC_3H_7$	H	75	151-54	5	-	1.5316	C, D
20245	$C_{11}H_{14}O_3$	2-Butanol, 4-(3,4-methylenedioxyphenyl)-	$-CH_2CH_2CHOHCH_3$	H	86	124-25	1	-	1.5344	D
20293	$C_{12}H_{16}O_3$	Piperonyl alcohol, alpha-tert-butyl-	$-CHOH-C(CH_3)_3$	H	72	173	20	-	1.5316	C, D
20338	$C_{11}H_{14}O_3$	Piperonyl alcohol, alpha-isopropyl-		H	69	123	2	-	1.5348	C, D
20381	$C_{12}H_{14}O_3$	Piperonyl alcohol, alpha-methallyl-		H	91	140-9	2	-	1.5501	D (2)
20382	$C_{12}H_{16}O_3$	Piperonyl alcohol, alpha-butyl-	$-CHOHCH_2CH_2CH_2CH_3$	H	74	141-50	1	-	1.5362	C, D
20383	$C_{13}H_{18}O_3$	Piperonyl alcohol, alpha-(1,1-dimethylpropyl)-		H	13	139-70	2	-	1.5448	C, D
20384	$C_{13}H_{18}O_3$	Piperonyl alcohol, alpha-pentyl-	$-CHOHCH_2CH_2CH_2CH_2CH_3$	H	68	158-61	3	-	1.5320	C, D
20416	$C_{14}H_{18}O_3$	Piperonyl alcohol, alpha-cyclohexyl-	$-CHOH-C_6H_{11}$	H	36	150	1	-	1.5559	C, D
20430	$C_{17}H_{18}O_3$	Piperonyl alcohol, alpha-3-phenylpropyl-	$-CHOHCH_2CH_2CH_2C_6H_5$	H	75	197	3	-	1.5775	C, D
20717	$C_{21}H_{26}O_4$	Chrysanthemumic acid, 6-propenylpiperonyl ester	$-CH=CHCH_3$	$-CH_2-OC-R''$	30	195-206	0.5	-	1.5438	E

20821	$C_{12}H_{17}NO_2$	Piperonylamine, N-butyl-	$-CH_2NHC_4H_9$	H	77	160-165	13	-	1.5320	I
20822	$C_{15}H_{25}NO_2$	Piperonylamine, N,N-dibutyl-	$-CH_2N(C_4H_9)_2$	H	77	116-124	0.5	-	1.5181	I
20823	$C_{17}H_{27}NO_2$	Piperonylamine, N-butyl-N-pentyl-	$-CH_2N(C_4H_9)C_5H_{11}$	H	46	121-125	0.3	-	1.5060	I
20838	$C_{15}H_{23}NO_2$	Piperonylamine, N-butyl-N-propyl-	$CH_2N(C_3H_7)C_4H_9$	H	79	128-132	2	-	1.5197	I
20848	$C_{14}H_{17}NO_3$	Cinnamamide, N,N-diethyl-3,4-methylenedioxy-	$-CH=CH-CON(C_2H_5)_2$	H	44	-	-	68-71	-	G (11, p. 249)
20854	$C_{10}H_{10}O_3$	2-Propen-1-ol,3-(3',4'-methylenedioxyphenyl)-	$-CH=CHCH_2OH$	H	100	-	-	78-80 (cis) 123° (trans(20))	-	D (11, p. 249)
20855	$C_{10}H_{12}O_3$	1-Propanol, 3-(3',4'-methylenedioxyphenyl)-	$-CH_2CH_2CH_2OH$	H	70	132	0.2	-	1.5420	D (11, p. 249)
20856	$C_{20}H_{24}O_4$	Chrysanthemumic acid, 3-(3',4'-methylenedioxyphenyl)-2-propenyl ester	$-CH=CHCH_2-OC(=O)-R''$	H	94	185-190	0.1	-	1.5528	E
20857	$C_{20}H_{26}O_4$	Chrysanthemumic acid, 3-(3',4'-methylenedioxyphenyl)propyl ester	$-CH_2CH_2CH_2-OC(=O)-R''$	H	89	170-173	0.03	-	1.5210	E
20863	$C_{10}H_{13}NO_2$	Piperonylamine, N-ethyl-	$-CH_2NHC_2H_5$	H	81	143-150	17	-	1.5340	I
20864	$C_{13}H_{19}NO_2$	Piperonylamine, N-ethyl-N-propyl-	$-CH_2N(C_2H_5)C_3H_7$	H	75	110-114	0.5	-	1.5161	I
20865	$C_{14}H_{21}NO_2$	Piperonylamine, N-butyl-N-ethyl-	$-CH_2N(C_2H_5)C_4H_9$	H	70	116-121	0.4	-	1.5133	I
20866	$C_{16}H_{25}NO_2$	Piperonylamine, N-butyl-N-isobutyl	$-CH_2N(C_4H_9\text{-iso})C_4H_9$	H	54	124	0.4	-	1.5253	I
20874	$C_9H_{10}O_3$	Piperonyl alcohol, alpha-methyl-	$-CHOHCH_3$	H	85	122	0.6	-	1.5103	C, D
20875	$C_{11}H_{11}ClO_2$	Piperonyl chloride, 6-propenyl-	$-CH_2Cl$	$-CH=CHCH_3$	50	120-30	1	-	-	A (10)
20906	$C_{11}H_{12}O_3$	Piperonyl alcohol,6-allyl-	$-CH_2OH$	$-CH_2CH=CH_2$	58	145-49	1.7	47-50	-	A (10)
20907	$C_{11}H_{10}O_3$	Piperonal, 6-allyl-	$-CHO$	$-CH_2CH=CH_2$	30	136-48	1.3	-	1.5692	B
20908	$C_{21}H_{26}O_4$	Chrysanthemumic acid, 6-allylpiperonyl ester	$-CH_2CH=CH_2$	$-CH_2-OC(=O)-R''$	89	189	0.8	-	1.5318	E
20909	$C_{13}H_{14}O_4$	Piperonyl alcohol, 6-allyl-, acetate	$-CH_2CH=CH_2$	$-CH_2OOCCH_3$	45	133-51	0.8	-	1.5318	A, D
20962	$C_{12}H_{11}NO_2$	Acetonitrile, 2-allyl-4,5-methylenedioxyphenyl	$-CH_2CN$	$-CH_2CH=CH_2$	69	120-45	1-2.5	-	1.5378	(19)
20963	$C_{11}H_{11}ClO_2$	Safrole, 6-(chloromethyl)-	$-CH_2Cl$	$-CH_2CH=CH_2$	41	148	3.5	42	-	A (10)
20964	$C_{19}H_{28}O_5$	Safrole, 6-[2(2-butoxyethoxy)ethoxy] methyl	$-CH_2CH=CH_2$	$-CH_2OCH_2CH_2OCH_2CH_2OC_4H_9$	47	402/	0.05	-	1.5075	J
20986	$C_7H_4Br_2O_2$	Benzene, 1,2-dibromo-4,5-methylenedioxy-	Br	Br	57	-	-	84-6	-	(12)
20988	$C_{11}H_{10}O_3$	Piperonal, 6-propenyl-	$-CHO$	$-CH=CHCH_3$	10	130-60	0.8	-	1.5542	B
20989	$C_{12}H_{11}NO_2$	Acetonitrile, 4,5-methylenedioxyphenyl-2-propenyl-	$-CH_2CN$	$-CH=CHCH_3$	52	129-44	0.6	-	1.5270	(19)

Table 1.--Continued

ENT No.	Empirical formula	Name	R	R'	Yield (%)	Boiling point ° C.	Boiling point mm/Hg	Melting point (° C.)	n_D^{25}	Method of preparation[1/]
20997	$C_{10}H_{11}BrO_2$	Benzene, 5-(2-bromopropyl)-1,2-methylenedioxy-	$-CH_2CHBrCH_3$	H	79	127	0.9	-	1.5610	(16)
21013	$C_{12}H_{14}O_4$	2-Propanol, 1-(3,4-methylenedioxyphenyl)-acetate	H	$-CH_2CH(CH_3)OCCH_3$ (O)	81	120-30	1	-	1.5208	C
21015	$C_{10}H_{12}O_3$	2-Propanol, 1-(3,4-methlenedioxyphenyl)-	$-CH_2CHOHCH_3$	H	89	not dist.	-	-	1.5305	D (16)
21016	$C_{11}H_{14}O_3$	1-Propanol, 2-piperonyl-	$-CH_2CH(CH_3)CH_2OH$	H	81	130-9	0.7	-	1.5338	(20, 23)
21017	$C_{12}H_{10}N_2O_5$	Barbituric acid, 5-piperonyl-	H		87	-	-	228-30	-	(7)
21019	$C_{20}H_{26}O_4$	Chrysanthemumic acid, ester with 1-piperonylethanol	H	$-CH_2CH(CH_3)OC-R''$ (O)	67	167-178	0.05	-	1.5182	E
21020	$C_{21}H_{28}O_4$	Chrysanthemumic acid, ester with 2-piperonyl-1-propanol-	H	$-CH_2CH(CH_3)CH_2OC-R$ (O)	83	196-200	0.8	-	1.5190	E
21029	$C_{19}H_{28}O_5$	Benzene, 4-[2-(2-butoxyethoxy)-ethoxy]methyl -1,2-methylenedioxy-5-propenyl-	$-CH=CH-CH_3$	$-CH_2OCH_2CH_2OCH_2CH_2OC_4H_9$	16	180-187	0.7	-	1.5096	J
21030	$C_{25}H_{28}O_4$	Chrysanthemumic acid, alpha-(p-methylphenyl)piperonyl ester	H		33	140-60	0.01	-	1.5160	E
21031	$C_{17}H_{22}O_6$	Succinic acid, 2-piperonyl-, 1-ethyl 4-propyl ester	H	$-CH_2CH(COOC_2H_5)CH_2COOC_3H_7$	14	189	0.7	-	1.5223	(1, 6)
21032	$C_{17}H_{22}O_6$	Succinic acid, 2-piperonyl-, 4-ethyl 1-propyl ester	H	$-CH_2-CH(COOC_3H_7)CH_2-COOC_2H_5$	33	190-9	2.5	-	1.5151	(1, 6)
21033	$C_{17}H_{22}O_6$	Succinic acid, 2-piperonyl-, 4-ethyl 1-isopropyl ester	H	$-CH_2-CH(COOCH(CH_3)_2)CH_2-COOC_2H_5$	17	202-6	2	102-3	-	(1, 6)

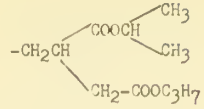
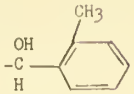
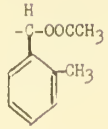
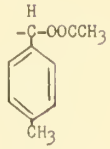
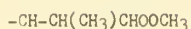
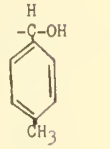
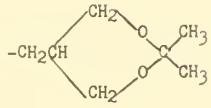
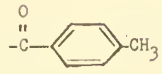
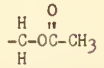
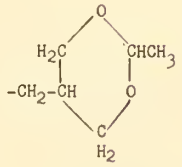
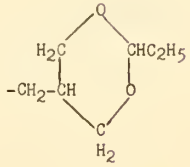
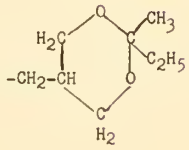
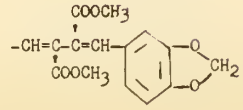
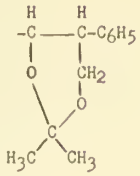
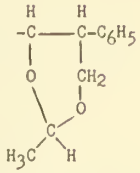
21034	$C_{18}H_{24}O_6$	Succinic acid, 2-piperonyl-, 1-isopropyl 4-propyl ester	H		14	201	1.5	97-99.5	-	(1, 6)
21037	$C_{15}H_{14}O_3$	Piperonyl alcohol, alpha-(o-methylphenyl)-		H	86	Not dist.		-	1.5901	D
21038	$C_{17}H_{16}O_4$	Piperonyl alcohol, alpha-(o-methylphenyl)-, acetate	H		79	169-174	0.2	-	1.5718	C
21039	$C_{17}H_{16}O_4$	Piperonyl alcohol, alpha-(p-methylphenyl)-, acetate	H		29	176	0.2	-	1.5695	C
21054	$C_{13}H_{14}O_4$	Cyclopropropanecarboxylic acid, 2-methyl-3-(3',4'-methylenedioxyphenyl)-, methyl ester		H	40	143-151	0.8	-	1.5394	(15)
21055	$C_{13}H_{14}O_4$	Cyclopropanecarboxylic acid, 2-piperonyl-, methyl ester		H	35	153-155	1	-	1.5307	(15)
21056	$C_9H_7NO_2$	Acetonitrile, 3,4-methylenedioxyphenyl	$-CH_2CN$	H	32	122	0.8	-	1.5478	(19)
21057	$C_{15}H_{14}O_3$	Piperonyl alcohol, alpha-(p-methylphenyl)-	H		86	Not dist.		-	1.5874	C
21127	$C_{11}H_{14}O_4$	1,3-Propanediol, 2-piperonyl-	$-CH_2CH(CH_2OH)_2$	H	83	-	-	91-3	-	J (14, 22)
21128	$C_{14}H_{18}O_4$	m-Dioxane, 2,2-dimethyl-5-piperonyl-	H		66	-	-	81-82	-	J (21)
21141	$C_{15}H_{12}O_3$	Benzophenone, 4-methyl-3',4'-methylenedioxy-		H	78	-	-	65-67.5	-	F
21172	$C_{19}H_{24}O_4$	Chrysanthemumic acid, 3,4-methylenedioxyphenethyl ester	H		100	152-165	0.3	-	1.5181	E (8)
21175	$C_8H_5BrO_3$	Piperonal, 6-bromo-	-CHO	Br	12	-	-	125-7	-	(18)

Table 1.--Continued

ENT No.	Empirical formula	Name	R	R'	Yield (%)	Boiling point		Melting point (° C.)	n_D^{25}	Method of preparation 1/
						° C.	mm/Hg			
21176	$C_{16}H_{16}O_3$	Piperonyl alcohol, alpha-methyl-alpha-(p-methylphenyl)-		H	45	158-165	1.2	-	1.6075	C, F
21177	$C_8H_6Br_2O_2$	Piperonyl bromide, 6-bromo-	$-CH_2Br$	Br	70	-	-	92-3	-	(17)
21184	$C_{10}H_9BrO_4$	Piperonyl alcohol, 6-bromo-, acetate		Br	96	-	-	81-82	-	C (10)
21194	$C_8H_7BrO_3$	Piperonyl alcohol, 6-bromo-	$-CH_2OH$	Br	quan.	-	-	89-90	-	(17)
21244	$C_9H_6BrNO_2$	Acetonitrile, (6-bromo-3,4-methylenedioxyphenyl)-	$-CH_2CN$	Br	70	-	-	71	-	(17)
21245	$C_7H_4Cl_2O_2$	Benzene, 1,2-dichloro-4,5-methylenedioxy-	Cl	Cl	19	-	-	82	-	(12)
21253	$C_{13}H_{16}O_4$	m-Dioxane, 2-methyl-5-piperonyl-		H	54	144-146	1	76-78	-	J (21)
21254	$C_{14}H_{18}O_4$	m-Dioxane, 2-ethyl-5-piperonyl-		H	64	150-153	0.8	66-67	-	J (21)
21255	$C_{15}H_{20}O_4$	m-Dioxane, 2-ethyl-2-methyl-5-piperonyl-		H	40	158	0.8	-	1.5351	J (21)
21256	$C_{18}H_{28}O_4$	Benzene, 4-[1-(2-ethylhexyloxy)-ethoxy]methyl-1,2-methylenedioxy-	H	$-CH_2O-CH(CH_3)-OCH_2CH(C_2H_5)C_4H_9$	60	154	0.8	-	1.4891	H
21257	$C_{12}H_{16}O_4$	Benzene, 4-(1-ethoxyethoxy)-methyl-1,2-methylenedioxy-	H	$-CH_2-O-CH(CH_3)OC_2H_5$	83	112-116	1.1	-	1.5021	H
21258	$C_{22}H_{18}O_8$	Succinic acid, 2,3-dipiperonylidene-, dimethyl ester	H		100	-	-	181-182	-	(9)

21274	$C_{12}H_{15}ClO_4$	Benzene, 4-[1-(2-chloroethoxy)-ethoxy]methyl-1,2-methylenedioxy-	H	$-CH_2O-CH(CH_3)OC_2H_4Cl$	83	137-156	0.7	-	1.5202	H
21275	$C_{14}H_{20}O_4$	Benzene, 4-(1-butoxyethoxy)methyl-1,2-methylenedioxy-	H	$-CH_2O-CH(CH_3)OC_4H_9$	71	131	0.6	-	1.4954	H
21276	$C_{14}H_{20}O_4$	Benzene, 4-(1-isobutoxyethoxy)methyl-1,2-methylenedioxy-	H	$-CH_2O-CH(CH_3)OC_4H_9$-(iso)	63	123	0.8	-	1.4938	H
21346	$C_{19}H_{20}O_4$	m-Dioxane, 2,2-dimethyl-4-(3',4'-methylenedioxyphenyl)-5-phenyl-	H		80	-	-	136-138	-	J (21)
21347	$C_{16}H_{16}O_4$	1,3-Propanediol, 1-(3',4'-methylenedioxyphenyl)-2-phenyl-	$-CHOHCH(CH_2OH)C_6H_5$	H	89	-	-	125-127	-	J (4)
21353	$C_{18}H_{18}O_4$	m-Dioxane, 2-methyl-4-(3',4'-methylenedioxyphenyl-5-phenyl-	H		60	200	0.7	109-111	-	J (21)

1/ Letters refer to methods described in the text and numbers to literature references.

2/ Distilled in molecular still.

Key to Biological Activity of Compounds Shown in Table 2

The classification given below is the same as that used by King (13) except for the synergistic data.

Toxicants

Mosquito larvae

1. Less than 50 percent at 10 p.p.m.
2. 50 to 94 percent at 10 p.p.m.
3. 95 to 100 percent at 10 p.p.m. but less than 50 percent at 1 p.p.m.
4. 50 to 100 percent at 1 p.p.m.

4A. 95 to 100 percent at 0.01 p.p.m.

Body lice

1. Ineffective
2. Effective (no survivors) on the initial exposure but ineffective on the second exposure started 1 day after treatment.
3. Effective on the second exposure but failed on or before the 10th day.
4. Effective for 10 days or more.

4A. Effective for 31 days or more.

Chiggers

1. Ineffective on initial test (not all down within 15 minutes).
2. Effective on initial test but ineffective after a 15-minute rinse.
3. Effective after the rinse but not after three washings.
4. Effective after three or more washings.

4A. Effective after five washings.

Synergists

Body lice and house flies

1. Ineffective - no decided synergist activity
3. Some synergism but less than standard.
4. Effective as standard.

Pyrethrins with sulfoxide was used as a standard in the body lice tests and allethrin with piperonyl butoxide in house fly tests.

Repellents

Mosquitoes (tests on cloth)

1. Ineffective on initial test (5 or more bites in 1 minute).
2. Effective for 1 to 5 days.
3. Effective for 6 to 10 days.
4. Effective for more than 10 days.

Table 2.--Biological activity of miscellaneous compounds containing the methylenedioxyphenyl structure.

ENT No.	Mosquito larvicide	Louse toxicant	Chigger toxicant	Mosquito repellent	Body lice synergist	House fly synergist
5688	1	1	1	1	-	3
5702	2	1	1	1	-	-
10502	1	1	2	1	4	3
16012	1	1	3	1	-	3
16016	1	1	1	1	-	3
20000	2	1	3	1	inef.	inef.
20085	1	4	4	1	inef.	inef.
20245	1	1	3	2	-	-
20293	1	1	3	4	-	-
20338	2	3	3	3	-	-
20381	1	1	3	2	-	-
20382	2	3	4	1	-	-
20383	1	3	4	1	-	-
20384	4	4	4	1	-	-
20416	2	3	3	1	-	-
20430	3	1	1	1	-	-
20717	4	4A	1	-	4	inef.
20821	1	3	3	-	-	-
20822	1	4A	4	-	-	-
20823	1	4A	4	-	-	-
20838	1	4	4	-	-	-
20848	2	1	-	1	-	-
20854	1	1	3	1	-	-
20855	1	1	3	1	-	-
20856	2	1	2	-	-	-
20857	2	1	2	-	-	inef.
20863	2	1	2	-	-	inef.
20864	2	3	4	-	-	inef.
20865	1	3	4	-	-	inef.
20866	1	3	3	-	-	inef.
20874	3	1	-	1	-	inef.
20875	1	3	4	-	-	-
20906	1	1	-	1	inef.	inef.
20907	1	3	-	1	inef.	inef.
20908	4	1	-	-	3	inef.
20909	1	1	-	1	inef.	inef.
20962	2	4A	-	1	4	3
20963	1	3	-	1	3	inef.
20964	2	1	-	-	4	4
20986	3	4	-	1	inef.	inef.
20988	2	4A	-	1	3	3
20989	1	4A	-	1	4	3
20997	1	3	-	1	3	inef.

Table 2.--Continued

ENT No.	Mosquito larvicide	Louse toxicant	Chigger toxicant	Mosquito repellent	Body lice synergist	House fly synergist
21013	1	1	-	1	3	inef.
21015	1	2	-	3	-	-
21016	1	4	-	1	-	-
21017	1	1	-	-	inef.	-
21019	2	1	-	1	4	inef.
21020	2	1	-	1	4	3
21029	2	1	-	-	3	3
21030	3	4	-	2	-	-
21031	1	1	-	1	3	-
21032	1	1	-	1	4	inef.
21033	1	1	-	1	3	-
21034	1	1	-	1	3	-
21037	1	1	-	1	-	-
21038	1	1	-	1	-	-
21039	1	1	-	1	-	-
21054	1	4	-	1	4	-
21055	1	4	-	1	4	-
21056	1	4	-	1	3	inef.
21057	1	1	-	1	-	-
21127	1	1	-	1	-	-
21128	2	1	-	-	4	4
21141	3	1	-	2	4	-
21172	4	1	-	-	3	4
21175	1	-	-	-	-	-
21176	3	1	-	1	1	1
21177	1	2	-	1	-	-
21184	1	1	-	1	inef.	-
21194	1	1	-	1	-	-
21244	1	1	-	1	-	-
21245	1	3	-	1	-	-
21253	2	-	-	-	4	3
21254	2	-	-	-	4	3
21255	2	-	-	-	4	3
21256	4	1	-	-	4	3
21257	2	2	-	-	3	3
21258	2	1	-	1	inef.	-
21274	1	2	-	-	3	3
21275	1	2	-	-	4	3
21276	1	2	-	-	4	3
21346	-	1	-	-	-	3
21347	-	1	-	1	-	-
21353	-	3	-	-	-	3